

together, and the overall and recent experience of clinical laboratories must be examined. Clinicians must be careful to correlate the direct amplification test results with the clinical aspects of each case; sometimes multiple testing or alternative types of information are of great value.

The direct amplification tests are an important advance in the diagnosis of tuberculosis. They do impose more work on laboratories and require more wisdom of clinicians, but if used properly, they can improve our ability to diagnose this disease, initiate therapy, and interrupt its transmission earlier than ever before. This can result in cutting the spread of tuberculosis in our community and the costs of health care.

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## Update on Treatment of Coccidioidomycosis

OF PATIENTS INFECTED with the fungus *Coccidioides immitis*, about two thirds will recover uneventfully, and in a third, symptomatic, self-limited pneumonitis will develop. Chronic coccidioidomycosis will develop in about 1% in the form of either progressive pulmonary or disseminated disease. The most common sites of extrapulmonary infection are the skin, bone, joints, lymph nodes, and central nervous system. Comprehensive review articles covering the clinical manifestations, diagnosis, and treatment of coccidioidomycosis have appeared recently, and, therefore, the focus of this discussion will be on advances that are likely to shape therapy in the coming years.

The development of a robust cellular immune response appears essential for a host to eliminate this fungus. Consequently, immunocompromised patients are at an increased risk for a progression to chronic forms of coccidioidomycosis and, should this progression occur, will require prolonged (possibly lifelong) therapy. Such patients typically have high titers of complement-fixing anticoccidioid antibodies and lack delayed-type hypersensitivity on skin testing. Similarly, patients who are without overt immunodeficiency and go on to have persistent disease commonly display this combination of anergy and increased

antibody titers, perhaps reflecting a selective inability to mount an effective immune response to this pathogen.

At present, the cornerstones of antifungal therapy are amphotericin B and the triazoles fluconazole and itraconazole. The incentive to use the triazoles is great because they are relatively nontoxic, well tolerated, and their use obviates the need for intravenous therapy. There have been no comparative trials of amphotericin B versus the azoles in the treatment of coccidioidomycosis, however, and the triazoles are not currently approved by the Food and Drug Administration for the treatment of this disease.

Although the vast majority of acute infections will resolve on their own, recent data from a nonrandomized trial suggest both that the primary illness may be truncated and that complications may be averted by early treatment of acute disease with an abbreviated course of a triazole (400 mg daily for 1 to 6 months). Such a practice seems prudent for those patients at risk for dissemination or with severe primary infections.

If the workup suggests progressive pulmonary or extrapulmonary disease, treatment is always indicated and invariably must be prolonged. Because meningitis can have devastating consequences and requires particularly aggressive therapy, it is imperative that its presence be ascertained before formulating a therapeutic plan. Symptoms of coccidioid meningitis are often subtle, and the threshold for performing a lumbar puncture must be low.

Extensive data now demonstrate the efficacy of using itraconazole and fluconazole for the treatment of progressive pulmonary and disseminated coccidioidomycosis. A recent trial, however, documented a high relapse rate, occurring in nearly 40% of patients, following the discontinuation of fluconazole therapy. A combination approach featuring initial surgical resection or the debridement of affected tissue when feasible—for example, for bronchopleural fistula or osteomyelitis—the instillation of amphotericin B locally when practical (especially with meningitis), and concurrent oral therapy with a triazole has gained favor. Once a response with combination therapy has been achieved, azole therapy alone is continued. Recent analyses have suggested that patients with meningitis and perhaps all patients with the acquired immunodeficiency syndrome and a diagnosis of progressive or disseminated coccidioidomycosis should continue on suppressive azole therapy for life.

Progress is being made on improving the antifungal armamentarium. Existing agents are being reformulated, such as the lipid forms of amphotericin B, which may allow for treatment with reduced toxicity. Second, itraconazole has been reformulated as an oral solution using the carrier cyclodextrin, and this appears to confer increased bioavailability. In addition, new triazole compounds continue to be developed and evaluated, such as SCH 56592. Furthermore, antifungal agents representing entirely new classes of compounds are nearing clinical trial. Nikkomycin Z prevents cell wall synthesis in a variety of fungi, including *Coccidioides immitis*, by inhibiting the enzyme chitin synthase. It appears fungicidal in studies of animals and is active when given orally. Echinocandins, such as

LY303366, which disrupt cell wall synthesis by inhibiting the enzyme  $\beta$ -(1,3)-glucan synthase, also appear promising. Immune modulators, which may ultimately allow the manipulation of the immune response in patients with disseminated disease, include interferon gamma and interleukin-12. Finally, progress is being made in the molecular characterization of the coccidioid antigens that are recognized during the humoral and cellular immune responses to infection. In addition to providing reagents that will allow easier diagnosis of infection, these studies should provide information crucial for the development of an effective vaccine against infection.

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## Role of Thoracoscopy in Thoracic Surgical Practice

THORACOSCOPY or the more commonly used term, video-assisted thoracic surgery (VATS), refers to the use of minimally invasive operative techniques employing television guidance to accomplish thoracic surgical procedures previously requiring thoracotomy. The primary aim of this approach is to avoid the perioperative morbidity associated with open thoracotomy. Most diagnostic pleural procedures and simple therapeutic VATS procedures, such as wedge resection of the lung, use two to three small (2.5-cm [1-in]) incisions to achieve access to the thoracic cavity through the rib interspaces. These sites of access allow the introduction of the thoracoscope camera, hand instruments, and endoscopic stapling tools. More complex procedures such as pulmonary lobectomy, esophageal procedures, and mediastinal procedures such as thymectomy usually need additional sites of intercostal access.

The following VATS approaches are accepted in present-day thoracic surgical practice.

Many pleural effusions remain idiopathic, despite attempts at diagnosis with less invasive techniques such as thoracentesis or pleural biopsy. Other malignant or benign pleural effusions may resist tube thoracostomy management alone. Video-assisted thoracoscopic techniques are successful in diagnosing 90% of cases of idiopathic effusion (most of which are malignant). Loculated pleural effusions, hemothoraces, and thoracic empyemata, for which tube thoracostomy treatment has failed, are also

readily controlled with VATS, with the added benefit of avoiding thoracotomy in more than 80% of patients.

The VATS approach is readily suited as an adjunct to cervical mediastinoscopy in the evaluation of mediastinal adenopathy. In patients with this disorder, VATS is an alternative to the anterior minithoracotomy procedure for evaluating adenopathy out of reach of cervical mediastinoscopy. This approach can also be a good alternative to thoracotomy for managing posterior mediastinal tumors and mediastinal cysts and for doing thoracic splachnicectomy and vagotomy.

Indeterminate noncalcified pulmonary nodules and undiagnosed diffuse pulmonary infiltrates are common thoracic problems often requiring surgical biopsy. Until the development of VATS, an open thoracotomy with its attendant morbidity was required. Closed-lung biopsy done with VATS techniques is a preferred approach to many of these processes. Although most pulmonary infiltrates are amenable to VATS, candidate pulmonary nodules for the VATS approach should be small (<3 cm in diameter), located in the outer third of the lung parenchyma, and without endobronchial extension. Among patients with low surgical risk, the early use of the VATS excisional biopsy approach avoids the time delay in management, technical complications, expense, and the unacceptable false-negative diagnostic rate associated with percutaneous and transbronchial biopsy procedures. Diagnostic accuracy is excellent, postoperative mortality negligible, and hospital stays usually about three days. When the lesion is diagnosed as being benign or metastatic malignant disease, thoracotomy can usually be avoided. If intraoperative frozen section analysis identifies a primary lung cancer, conversion to a muscle-sparing minithoracotomy or the use of the VATS technique to accomplish anatomic lobectomy and mediastinal nodal dissection is indicated.

Pulmonary lobectomy and mediastinal nodal staging remain the gold standard of management for stage 1 lung cancer, but VATS wedge resection of peripheral small lung cancers can be an alternative to open surgical resection for patients with impaired cardiopulmonary reserve. Patient survival has been equivalent to that in patients with similar stage disease having lobectomy; the local recurrence rate is higher, however. As a compromise procedure, it appears to be reasonable. Nevertheless, we use this approach only with poor-risk patients who could not withstand the rigors of thoracotomy and lobar resection.

Lung volume reduction surgery has been shown to restore a more normal elasticity of emphysematous lungs and to improve the efficiency of the muscles of respiration. This operation has been described using either an open sternotomy approach or VATS techniques. Equivalent functional improvement has been noted with either approach, but the use of VATS avoids the morbidity associated with dividing the sternum.

Video-assisted thoracic surgical procedures are a growing technical component in the operative armamentarium of most thoracic surgeons today. Some centers are using VATS techniques in nearly 60% of their thoracic surgical interventions. It is a good approach to a variety of